

=> d his

(FILE 'HOME' ENTERED AT 13:11:01 ON 10 OCT 2001)

FILE 'WPIDS' ENTERED AT 13:11:11 ON 10 OCT 2001
E EP 97-393111/AP, PRN 25

E EP 97-303111/AP, PRN 25

L1 1 S E3

FILE 'USPATFULL' ENTERED AT 14:14:38 ON 10 OCT 2001

L2 177 S 75330-75-5/RN

L3 103 S 81093-37-0/RN

L4 75 73573-88-3/RN

L5 115 79902-63-9/RN

L6 246 S L2 OR L3 OR L4 OR L5

L7 391313 S CRYSTAL?

L8 107 S L6 AND L7

L9 101464 S ETHYL ACETATE

L10 11103 S ETHYLACETATE

L11 104312 S L9 OR L10

L12 79 S L11 AND L8

FILE 'WPIDS' ENTERED AT 14:25:38 ON 10 OCT 2001

L13 328 S LOVASTATIN OR PRAVASTATIN OR MEVATATIN OR SIMVASTATIN OR
COMP

L14 41 S MEVASTATIN

L15 329 S L13 OR L14

L16 24 L15 AND L7

L17 9 S L11 AND L16

=> log hold

COST IN U.S. DOLLARS

SINCE FILE

ENTRY

TOTAL

SESSION

FULL ESTIMATED COST

64.10

133.37

SESSION WILL BE HELD FOR 60 MINUTES

STN INTERNATIONAL SESSION SUSPENDED AT 14:33:35 ON 10 OCT 2001

Connection closed by remote host

L14 ANSWER 3 OF 54 CAPLUS COPYRIGHT 2001 ACS
AN 2001:416764 CAPLUS
DN 135:18608
TI Process for recovering statin compounds from a fermentation broth
IN Keri, Vilmos; Deak, Lajos; Forgacs, Ilona; Szabo, Csaba; Nagyne, Edit
Arvai
PA Biogal Gyogyszergyar Rt, Hung.; Teva Pharmaceuticals USA, Inc.
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

MPA

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---------------|--|----------|-----------------|----------|
| PI | WO 2001039768 | A1 | 20010607 | WO 2000-US32391 | 20001128 |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| | RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |

PRAI US 1999-168056 P 1999/1130

AB A novel process for recovering a compd. from a fermn. broth that includes the stages of forming an enriched soln. of the compd. by extn., obtaining a salt of the compd. from the enriched soln., purifying a salt of the compd. and exchanging the salt of the compd. to a metal salt of the compd.

is disclosed. Thus, pravastatin was extd. by iso-Bu acetate from fermn. broth which had been acidified to pH 2.5 by sulfuric acid. The the pH of the solvent ext. was then adjusted to 11 by the addn. of aq. ammonium hydroxide and the resulting aq. pravastatin soln. was re-acidified and then back extd. with iso-Bu acetate. After the iso-Bu acetate ext. had been partially dried and decolorized with activated charcoal, ammonia gas was added to the headspace of the soln. until all pptn. ceased. The pptd.

ammonium pravastatin salt was collected by filtration, washed with solvents, dild. in water, acetone and iso-Bu acetate, crystd. by the addn. of solid ammonium chloride. The crystd. ammonium pravastatin further crystd. in isobutanol. The ammonium pravastatin salt crystals were then dissolved in a water and iso-Bu acetate was added. The soln. was acidified to ph 2-4 with sulfuric

acid, washed with water and the pravastatin was converted to its sodium slat by the intermittent addn. of sodium hydroxide. Excess sodium ions were removed by ion exchange and the sodium pravastatin salt was crystd. in a water/acetonitrile/acetone solvent. A sodium pravastatin yield of 65% with a purity of 99.3% was obtained with this process.

RE.CNT 4

RE

- (1) Furuya; US 5153124 A 1992 CAPLUS
- (2) Gist-Brocades; WO 9837220 A 1998 CAPLUS
- (3) Gist-Brocades; WO 991049 A 1999
- (4) Teva Pharmaceuticals USA Inc; WO 0046175 A1 2000 CAPLUS